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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/831,627 | 09/14/2001 | Luigi Naldini | 131.14-US-WO | 5935 |

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| EXAMINER | |
|---|---|
| ZEMAN, ROBERT A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1645 | |

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9

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/831,627 | NALDINI ET AL. | |
| | Examiner | Art Unit | |
| | Robert A. Zeman | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 September 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-3* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Information Disclosure Statement*

The information disclosure statement filed on 5-13-2002 is acknowledged. An initialed copy is attached hereto.

### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-16 of U.S. Patent No. 5,994,136. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons. The instant claims are drawn to methods of amplifying (propagating) an envelope defective retrovirus by "exposing" said retrovirus to a cell that comprises a gene that encodes a virus envelope that complements said retrovirus. The instant claims recite no limitations on the form of said envelope gene (i.e. integrated in cell genome, in a plasmid etc.). The instant claims merely require that the envelope defective virus is amplified (claim 1), that

the propagated virus comprises the envelope encoded by the gene within the cell and that said envelope is expressed by said cell. Patent 5,994,136 recites in the aforementioned claims methods for producing recombinant HIV vectors (a retrovirus) wherein a cell is transformed with an HIV packaging plasmid (i.e. an envelope defective retrovirus) and an expression plasmid encoding an envelope gene. The expression vector allows the cell to express envelope proteins on their membrane surfaces. Hence, when the HIV vector is expressed the resulting "envelope defective retrovirus" is "exposed" to a cell comprising a virus envelope gene. Moreover, since said virus envelope proteins encoded by said gene will be expressed on the cell surface, the "progeny" virus will have said envelope proteins on its surface since the replication cycle of retroviruses includes budding through the cell membrane of the infected cell. Consequently, claims 13-16 of U.S. Patent No. 5,994,136 anticipate, and hence render obvious, the rejected claims.

Claims 1-3 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-9 of U.S. Patent No. 6,428,953. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to methods of amplifying (propagating) an envelope defective retrovirus by "exposing" said retrovirus to a cell that comprises a gene that encodes a virus envelope that complements said retrovirus. The instant claims recite no limitations on the form of said envelope gene (i.e. integrated in cell genome, in a plasmid etc.). The instant claims merely require that the envelope defective virus is amplified (claim 1), that the propagated virus comprises the envelope encoded by the gene within the cell and that said envelope is expressed

by said cell. Patent No. 6,428,953 recites in the aforementioned claims methods for producing recombinant lentivirus vectors (a retrovirus) wherein a cell is transformed with an lentivirus packaging plasmid (i.e. an envelope defective retrovirus) and a expression plasmid encoding an envelope gene. The expression vector allows the cell to express envelope proteins on their membrane surfaces. Hence, when the lentivirus vector is expressed the resulting "envelope defective retrovirus" is "exposed" to a cell comprising a virus envelope gene. Moreover, since said virus envelope proteins encoded by said gene will be expressed on the cell surface, the "progeny" virus will have said envelope proteins on its surface since the replication cycle of retroviruses includes budding through the cell membrane of the infected cell. Consequently, claims 6-9 of U.S. Patent No. 6,428,953 anticipate, and hence render obvious, the rejected claims.

***Claim Rejections - 35 USC § 112***

Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "exposing" renders claim 1 vague and indefinite since it is unclear what limitation is meant to be conferred by said phrase. Said term is not explicitly defined in the specification. Said term is being interpreted to mean any type of contact between the cell and the envelope defective retrovirus (e.g. when a mature particle within a packaging cell becomes enveloped).

The phrase "wherein said virus envelope protein is expressed at the surface of a virus particle produced by said cell" renders claim 2 vague and indefinite since it is unclear what limitation is meant to be conferred by said phrase. Retroviruses obtain their envelopes when they bud through the cellular membrane. In order for an envelope-defective retrovirus to obtain an envelope, the "infected cell" must express the envelope proteins on its surface. Moreover, the term "expressed" as it applies to virions is confusing as said virions do not actively express envelope proteins. Said proteins are produced (expressed) by the infected cells.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Sadaie et al. (Virology, 1992, Vol. 187, pages 604-611).

The instant claims are drawn to methods of amplifying (propagating) an envelope defective retrovirus by "exposing" said retrovirus to a cell that comprises a gene that encodes a virus envelope that complements said retrovirus. The instant claims recite no limitations on the

form of said envelope gene (i.e. integrated in cell genome, in a plasmid etc.). The instant claims merely require that the envelope defective virus is amplified (claim 1), that the propagated virus comprises the envelope encoded by the gene within the cell and that said envelope is expressed by said cell.

Sadaie et al. disclose the production of an envelope defective HIV-1 virus and Env-producing plasmids (see abstract and materials and methods section on page 605). Sadaie et al. further disclose that the defective virus and the Env-producing plasmid is transfected into cells (see methods section on page 605). Said transfected cells produce virus particles with the wild-type phenotype (i.e. viruses have an envelope) [see page 607, 2nd column]. Moreover, since the progeny virus has the wild-type phenotype, it is apparent that the envelope proteins encoded by envelope "gene" is expressed on the cell surface since the replication cycle of retroviruses includes budding through the cell membrane of the infected cell. Consequently, Sadaie et al. anticipates all the limitations of the instant claims.

Claims 1-3 are rejected under 35 U.S.C. 102(e) as being anticipated by Naldini et al. (U.S. Patent No. 5,994,136).

The instant claims are drawn to methods of amplifying (propagating) an envelope defective retrovirus by "exposing" said retrovirus to a cell that comprises a gene that encodes a virus envelope that complements said retrovirus. The instant claims recite no limitations on the form of said envelope gene (i.e. integrated in cell genome, in a plasmid etc.). The instant claims merely require that the envelope defective virus is amplified (claim 1), that the propagated virus

comprises the envelope encoded by the gene within the cell and that said envelope is expressed by said cell.

Naldini et al. disclose methods for producing recombinant HIV vectors (a retrovirus) wherein a cell is transformed with an HIV packaging plasmid (i.e. an envelope defective retrovirus) and an expression plasmid encoding an envelope gene. The expression vector allows the cell to express envelope proteins on their membrane surfaces. Hence, when the HIV vector is expressed the resulting "envelope defective retrovirus" is "exposed" to a cell comprising a virus envelope gene. Moreover, since said virus envelope proteins encoded by said gene will be expressed on the cell surface, the "progeny" virus will have said envelope proteins on its surface since the replication cycle of retroviruses includes budding through the cell membrane of the infected cell (see column 2, lines 63 to column 3, line 9, column 6, lines 50-65 and claim 13). Consequently, Naldini et al. anticipates all the limitations of the rejected claims.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Ory et al. (PNAS, 1996, Vol. 93, pages 11400-11406 – IDS-8).

The instant claims are drawn to methods of amplifying (propagating) an envelope defective retrovirus by "exposing" said retrovirus to a cell that comprises a gene that encodes a virus envelope that complements said retrovirus. The instant claims recite no limitations on the form of said envelope gene (i.e. integrated in cell genome, in a plasmid etc.). The instant claims merely require that the envelope defective virus is amplified (claim 1), that the propagated virus

comprises the envelope encoded by the gene within the cell and that said envelope is expressed by said cell.

Ory et al. disclose a packaging cell line for the production of high titer retroviruses with VSV G protein (envelope protein) [see abstract]. Ory et al. further disclose the transfection of cells with a retroviral vector (MuMLV-Env defective) and a plasmid encoding VSV-G envelope protein (see page 11401, 1st column and page 11403). Ory et al. also disclose that said cells expressed VSV-G on its surface (see page 11401, 2nd column and page 11403). The resulting "psuedotypes" (i.e. viruses produced by the transfected cells) contain VSV-G envelope proteins on their surface (see pages 11405-11406). Consequently, Ory et al. anticipates all the limitations of the rejected claims.

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert A. Zeman
August 17, 2004